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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,572	01/14/2004	Sharon Cohen-Vered	68518-A/JPW/GJG/JBC	5919

7590 09/22/2006

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New York, NY 10036

EXAMINER

DESAI, ANAND U

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 09/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/758,572

Applicant(s)

COHEN-VERED ET AL.

Examiner

Anand U. Desai, Ph.D.

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on June 30, 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-19, 21, 31, 32, 41-43, 52, 53 and 57-61 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-19, 21, 31, 32, 41-43, 52, 53 and 57-61 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>20060630</u> . | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

1. This office action is in response to Amendment filed on June 30, 2006. Claims 1-19, 21, 31, 32, 41-43, 52, 53, and 57-61 are currently pending and are under examination.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### *Double Patenting*

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-19, 21, 31, 32, 41, 42, 52, 53, and 57-61 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14, 16, 24, 25, 27, 36, 37, 47, and 52 of copending Application No. 10/758,397 (U.S. Patent Application Publication 2005/0008634 A1).

The rejections were explained in the previous Office action mailed June 6, 2005.

***Claim Rejections - 35 USC § 103***

5. Claims 1-4, 7, 8, 11, 19, 21, and 31 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Mozes U.S. 2004/0127408 A1 (Priority date = February 26, 2001) in view of Hora et al. U.S. Patent 5,997,856.

6. Claims 5, and 6 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Mozes U.S. 2004/0127408 A1 (Priority date = February 26, 2001) in view of Hora et al. U.S. Patent 5,997,856 as applied to claim 1-4, 7, 8, 11, 31, 42, 53, 57, and 59-61 above, and further in view of Anderson, B.D. and Flora, K.P (Chapter 34, pages 739-754, The Practice of Medicinal Chemistry, edited by Camille Georges Wermuth, Academic Press 1996).

7. Claims 9, 10, and 12-18 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Mozes U.S. 2004/0127408 A1 (Priority date = February 26, 2001) in view of Hora et al. U.S. Patent 5,997,856 as applied to claim 1-4, 7, 8, 11, and 31 above, and further in view of Stella et al. U.S. Patent 5,134,127.

The rejections were explained in the previous Office action mailed December 27, 2005.

***Response to Arguments***

8. Applicants' state the obviousness rejection of record is fundamentally deficient for failing to explain the motivation to combine Mozes and the '856 patent. Applicants' state there is nothing of record except hindsight, motivating the combination of the peptide of Mozes with any solubility enhancer, much less the ones of the '856 patent. Applicants' state the current record fails to identify a suggestion in the prior art to combine the recited peptide with any solubility

enhancing agent, much less a cyclodextrin. Applicants' state there is no reason of record explaining the selection of cyclodextrin over any other of the multitude of available solubility-enhancing agents. Applicants' state  $\beta$ -cyclodextrins were known to have less than desirable pharmaceutical properties. Applicants' state even if Mozes and the '856 patent were combined, there was no expectation of success. Applicants' state that nothing more than an "obvious to try" rationale has been presented in support of the rejection or record. Applicants' state the further limiting claims are not remedied by the additional references cited.

Applicant's arguments filed June 30, 2006 have been fully considered but they are not persuasive. Mozes does disclose the modification of the pharmaceutical properties of the peptide, such as solubility (see [0088]). Mozes describes the crosslinking of the peptide with macromolecular carriers and the manufacture of a pharmaceutical composition with the peptide and a pharmaceutically acceptable carrier (see [0099], [0100], and [0102]). Hora et al. describes the solubilization and/or stabilization of multiple polypeptides using cyclodextrin. Hora et al. describes a light scattering assay to see if lyophilized compositions with or without cyclodextrin stabilizer can produce clear solutions upon reconstitution. The composition is lyophilized using a LSL lyolab lyophilizer with a primary and secondary drying step. A value below 500 is a good and clear solution, a value in the range of 500-1000 represents a marginal solution, and scattering values > 1000 are unacceptable solutions (see col. 19, line 65 – col. 20, line 41). IL-2 compositions with hydroxypropyl-cyclodextrin display over 800-fold improvement in reconstitution. The IL-2 composition has a light scattering value of 66 with cyclodextrin versus a value of 558 without cyclodextrin. Insulin without cyclodextrin has no light scattering value, because the lyophilized plug did not dissolve, whereas the Insulin with cyclodextrin produces a

good value and clear solution upon reconstitution. TNF without cyclodextrin forms 3-5% dimmers in 4 weeks at 37°C, whereas TNF with cyclodextrin has no appreciable dimmers. The m-CSF values for the compositions have a 135-fold improvement in the presence of cyclodextrin when reconstitution (see Table 2, part A and B). Hora et al. describe the benefit of substituted  $\beta$ -cyclodextrins as compared to unsubstituted  $\beta$ -cyclodextrins. The light scattering value of a substituted  $\beta$ -cyclodextrins composition is 66, whereas the unsubstituted cyclodextrin is approximately 300 (see col. 22, line 22-31). It would have been obvious to one of ordinary skill in the art at the time of the invention was made to use the sulfobutyl ether substituted  $\beta$ -cyclodextrins to solubilize the pharmaceutical composition because Stella et al. do describe enhanced aqueous solubilization, reduced toxicity, and reduced membrane disruption of the sulfobutyl ether substituted  $\beta$ -cyclodextrins (see U.S. Patent '127, col. 3, lines 9-16).

### *Conclusion*

9. No claims are allowed.
10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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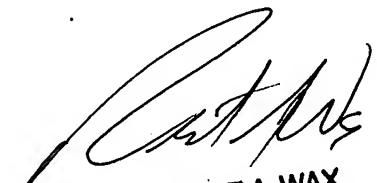
however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

September 18, 2006



ROBERT A. WAX  
PRIMARY EXAMINER